PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Case 21478	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/10838	International filing date *(day/month/year)* 30.09.2003	Priority date *(day/month/year)* 07.11.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/353, A61K31/16, A61K31/20, A61K31/385, A61K31/575, A61K31/12, A61P3/04, A61P3/10, A23L1/30, A61K31/00		
Applicant ROCHE VITAMINS AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27.05.2004	15.02.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Zimmer, B Telephone No. +49 89 2399-8600

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/10838

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-17 as originally filed

Claims, Numbers

1-20 received on 02.10.2004 with letter of 30.09.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 20 with regard to industrial applicability

because:

☒ the said international application, or the said claims Nos. 20 with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-20
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-20
Industrial applicability (IA)	Yes:	Claims	1-19
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 20 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Art. 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability

1. Reference is made to the following documents:

D6: WO 02/072086 A (CONSORZIO PER GLI STUDI UNI ;SUZUKI HISANORI (IT)) 19 September 2002 (2002-09-19)
D7: EP-A-1 177 789 (ROCHE VITAMINS AG) 6 February 2002 (2002-02-06)
D10: MCCARTY M F: "Hepatothermic therapy of obesity: Rationale and an inventory of resources" MEDICAL HYPOTHESES 2001 UNITED KINGDOM, vol. 57, no. 3, 2001, pages 324-336, XP009030758 ISSN: 0306-9877

2. Novelty (Art. 33(2) PCT)

None of the cited prior art documents discloses compositions comprising EGCG and at least one of pantethine and phytanic acid nor their medical use.
As a result, in view of the cited prior art the subject-matter of claims 1-20 of the present application seems to be novel (Art. 33(2) PCT).

3. Inventive Step (Art. 33(3) PCT)

Although the subject-matter of the present application seems to be novel in view of the cited prior art it does not involve an inventive step for the following reasons:

Prior art document D6 discloses the use of EGCG for the treatment of diabetes

and obesity (claim 3); from D7 the use of phytanic acid for the treatment of diabetes mellitus and syndrome X is known (claim 1) and prior art document D10 discloses the use of pantethine and green tea polyphenols for the treatment of obesity (abstract and p. 331, left col., last para.).

According to the description of the present application (p. 3, l. 24/25) the claimed combination of components leads to an additive/ synergistic effect. The present application, however, does not provide any proof for this alleged effect.
Therefore, the selection of EGCG and at least one of pantethine and phytanic acid in the compositions of the present application seems to be arbitrary and cannot "prima facie" be regarded as inventive as no convincing evidence (eg comparison tests showing an effect not derivable from the closest prior art) has been presented in order to show that an inventive step is necessary to use the claimed subject-matter for the solution of the posed problem.
If an inventive step is to be based on the presence of an unexpected effect this has to be proven by technical evidence.

Therefore, the claimed combinations of components and their use according to independent claims 1, 14 15 and 20 of the present applications are considered as obvious options for a person skilled in the art in view of the cited prior art.

Dependent claims 2-13 and 16-19 do not appear to contain any additional features which involve an inventive step when combined with the subject-matter of any claim to which they refer. Dependent claims are only allowable when related to a patentable independent claim (Rule 6.4 PCT).

As a result, the subject-matter of claims 1-20 does not seem to involve an inventive step (Art. 33(3) PCT).

4. Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 2004/ 017766 (D11)	04.03.2004	18.08.2003	23.08.2002

The above listed document was published after the priority date of the present ap-

plication (07.11.2002) and therefore does not belong to the state of the art according to Rule 64 (3) PCT. However, said document claims a priority date earlier than the priority date of the present application and may thus become relevant in later regional phases.
D11 discloses the same compositions and uses as claimed in the present application (claims 1-20); therefore, D11 might become highly relevant in terms of novelty for the subject-matter of claims 1-20 of the present application.

5. Further remarks

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in documents D6, D7 and D10 is not mentioned in the description, nor are these documents identified therein.

6. For the assessment of the present claim 20 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

What is claimed is :

1. A composition for the treatment or prevention of type 2 diabetes in those individuals with pre-diabetes, or impaired glucose tolerance (IGT) or obesity comprising at least two components selected from EGCG, pantethine or a metabolite thereof, phytanic acid, lipoic acid, policosanol and coenzyme Q-10.

2. A composition for the treatment or prevention of type 2 diabetes in those individuals with pre-diabetes, or impaired glucose tolerance (IGT) or obesity comprising at least two components selected from EGCG, pantethine or a metabolite thereof, phytanic acid, lipoic acid and coenzyme Q-10.

3. A composition as in claim 1 or 2 wherein EGCG and pantethine are present.

4. A composition as in claim 1 or wherein EGCG and phytanic acid are present.

5. A composition as in claim 1 or 2 wherein pantethine and phytanic acid are present.

6. A composition as in claim 3 or 4 containing EGCG in an amount sufficient to administer to a subject a daily dosage of 0.3 mg per kg body weight to about 30 mg per kg body weight.

7. A composition as in claim 3 or 5 containing pantethine in an amount sufficient to administer to a subject a daily dosage of 1 mg per kg body weight to about 50 mg per kg body weight.

8. A composition as in claim 4 or 5 containing phytanic acid in an amount sufficient to administer to a subject a daily dosage of 1 mg per kg body weight to about 100 mg per kg body weight.

9. A composition as in any one of claims 1-8 wherein lipoic acid is present.

10. A composition as in claim 9 wherein lipoic acid is present in an amount sufficient to administer to a subject a daily dosage of 0.3 mg per kg body weight to about 30 mg per kg body weight.

11. A composition as in any one of claims 1-10 wherein coenzyme Q-10 is present.

12. A composition as in claim 11 wherein coenzyme Q-10 is present in an amount sufficient to administer to a subject a daily dosage of 0.01 mg per kg body weight to about 30 mg per kg body weight.

13. A composition as in any one of claims 1-12 wherein policosanol is present.

14. A composition as in claim 13 wherein policosanol is present in an amount sufficient to administer to a subject a daily dosage of 0.002 mg per kg body weight to about 1.5 mg per kg body weight.

15. A composition as in any one of claims 1-14 which is in dosage unit form.

16. A composition as in claim 15 wherein the dosage unit form is a solid dosage unit form.

17. A composition as in claim 16 wherein the dosage unit form contains about 10 mg to about 500 mg of EGCG.

18. A composition as in claim 16 wherein the dosage unit form contains about 20 mg to about 1000 mg of pantethine.

19. A composition as in claim 16 wherein the dosage unit form contains about 30 mg to about 500 mg of phytanic acid.

20. A composition as in any one of claims 1-14 which is a food or beverage or a supplement composition for a food or beverage.

21. A food or beverage comprising at least two components selected from EGCG, pantethine or a metabolite thereof, phytanic acid, lipoic acid, policosanol and coenzyme Q-10.

22. The use of at least two components selected from EGCG, pantethine or a metabolite thereof, phytanic acid, lipoic acid, policosanol and coenzyme Q-10 in the manufacture of a nutraceutical composition.

23. The use as in claim 22 of a combination of EGCG and pantethine, or EGCG and phytanic acid, or pantethine and phytanic acid, said EGCG being used in an amount sufficient to provide a daily dosage of 0.3 mg per kg body weight to about 30 mg per kg body weight of the subject to which it is to be administered, said pantethine being used in an amount sufficient to provide a daily dosage of 1.0 mg per kg body weight to about 50 mg per kg body weight of the subject to which it is to be administered and said phytanic acid being used in an amount sufficient to provide a daily dosage of 1.0 mg per kg body weight to about 100 mg per kg body weight of the subject to which it is to be administered

24. The use as in claim 23 wherein the nutraceutical composition is a food or beverage, or a supplement composition for food or beverage.

25. The use as in claim 23 wherein the nutraceutical composition is intended for the treatment of both type 1 and 2 diabetes, and for the prevention of type 2 diabetes in those individuals with pre-diabetes, or impaired glucose tolerance (IGT) or obesity.

26. The use as in claim 23 wherein the nutraceutical composition is a pharmaceutical composition for the treatment of both type 1 and 2 diabetes, and for the prevention of type 2 diabetes in those individuals with pre-diabetes, or impaired glucose tolerance (IGT) or obesity.

27. A method for the treatment of both type 1 and 2 diabetes, and for the prevention of type 2 diabetes in those individuals with pre-diabetes, or impaired glucose tolerance (IGT) or obesity which comprises administering to a subject in need of such treatment at least two components selected from EGCG, pantethine or a metabolite thereof, phytanic acid, lipoic acid, policosanol and coenzyme Q-10.